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Original Research Article

Gene Expression of Thyroid-Stimulating Hormone Receptor (TSHR) in Patients with Hyperthyroidism and Hypothyroidism

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Abstract: Thyroid disorders are among the most common endocrine diseases and often involve dysregulation of thyroid hormone production and immune responses. The thyroid-stimulating hormone receptor (TSHR) gene plays a critical role in regulating thyroid gland function. Alterations in TSHR gene expression may contribute to the development of thyroid dysfunction. This study aimed to evaluate TSHR gene expression levels in patients with hyperthyroidism and hypothyroidism compared with healthy controls. Sixty individuals were included and divided into three groups: hyperthyroid patients (n = 20), hypothyroid patients (n = 20), and healthy control subjects (n = 20). TSHR gene expression was analyzed using quantitative real-time PCR (qRT-PCR). Statistical analysis revealed a highly significant difference ($P < 0.01$) among the studied groups. The hyperthyroid group showed significantly higher TSHR gene expression (3.4988 ± 1.3906) compared with the hypothyroid group (0.6509 ± 0.2462) and the control group (1.1190 ± 0.4155). These findings indicate that increased TSHR gene expression may be associated with hyperthyroid conditions and could play a role in the pathogenesis of autoimmune thyroid diseases.

Keywords: TSHR Gene, Gene Expression, Hyperthyroidism, Hypothyroidism, Thyroid Disorders.

INTRODUCTION

Thyroid disorders are prevalent endocrine diseases affecting millions of individuals worldwide. These conditions include hyperthyroidism and hypothyroidism, both of which result from disturbances in thyroid hormone production and regulation. Thyroid hormones are essential for metabolic processes, growth, and development (Antonelli *et al*., 2015).

The thyroid-stimulating hormone receptor (TSHR) is a G protein–coupled receptor located on the surface of thyroid follicular cells and plays a key role in mediating the effects of thyroid-stimulating hormone (TSH). Activation of this receptor stimulates thyroid hormone synthesis and secretion as well as thyroid cell growth. The TSHR gene encodes this receptor and is therefore essential for maintaining normal thyroid function [1].

Alterations in TSHR gene expression may contribute to thyroid dysfunction. In autoimmune thyroid diseases such as Graves' disease, antibodies stimulate the TSH receptor, leading to excessive thyroid hormone production and hyperthyroidism. Conversely, hypothyroidism may occur due to autoimmune destruction of thyroid tissue, as observed in Hashimoto's thyroiditis [4]. Therefore, investigating TSHR gene expression may provide valuable insight into the molecular mechanisms underlying thyroid disorders.

METHODOLOGY

Study Population: This study included 60 participants, divided into three groups:

- Hyperthyroid patients (n = 20)
- Hypothyroid patients (n = 20)
- Healthy control subjects (n = 20)

Patients were diagnosed based on clinical examination and laboratory tests measuring thyroid hormone levels.

Sample Collection: Approximately 5 mL of venous blood was collected from each participant. Samples were processed for molecular analysis.

RNA Extraction and Gene Expression Analysis:

Total RNA was extracted from blood samples using standard RNA extraction protocols. The extracted RNA was converted into complementary DNA (cDNA) using reverse transcription., TSHR gene expression levels were measured using quantitative real-time PCR (qRT-PCR). Relative gene expression levels were calculated using the comparative Ct method [6, 2].

RESULTS AND DISCUSSION

Table 1: The levels of TSHR in HYPER, HYPO and Control Groups

Groups	Mean	S.D	S.E.	LSD	P. Value
HYPO (n=20)	0.6509[a]	0.2462	0.0550	**0.5381**	**<0.001****
HYPER (n=20)	3.4988[b]	1.3906	0.3110		
Control (n=20)	1.1190[a]	0.4155	0.0929		

S.D. = Standard Deviation, S.E. = Standard Error
Averages that share the same alphabet are not significantly difference between them according to the LSD test.
** The differences are significant at the 0.01 level.

The gene expression levels of thyroid-stimulating hormone receptor (TSHR) in hyperthyroid, hypothyroid, and control groups are shown in Table 1. Statistical analysis revealed a highly significant difference ($P < 0.01$) among the studied groups. The hyperthyroid group exhibited significantly higher TSHR gene expression (3.4988 ± 1.3906) compared with the hypothyroid group (0.6509 ± 0.2462) and the control group (1.1190 ± 0.4155). Meanwhile, the hypothyroid and control groups shared the same statistical letter according to the LSD test, indicating that the difference between these two groups was not statistically significant.

The increased expression of the TSHR gene in hyperthyroid patients may reflect enhanced stimulation of thyroid follicular cells and increased receptor signaling activity. The TSH receptor plays a central role in regulating thyroid hormone synthesis and secretion. When TSH binds to this receptor, intracellular signaling pathways such as cyclic AMP (cAMP) are activated, promoting thyroid hormone production and thyroid cell growth [1]. Therefore, increased expression of the TSHR gene may lead to increased receptor availability and enhanced thyroid gland responsiveness.

The present findings are consistent with several previous studies investigating the molecular mechanisms of hyperthyroidism. Reported that hyperthyroidism, particularly Graves' disease, is strongly associated with abnormal activation of the TSH receptor caused by thyroid-stimulating autoantibodies. These antibodies mimic the action of TSH and continuously stimulate the receptor, resulting in excessive thyroid hormone production and increased metabolic activity [3].

Similarly, previous study demonstrated that the TSH receptor is the primary autoantigen involved in autoimmune hyperthyroidism. Their study suggested that increased receptor activity and gene expression may contribute to the pathological stimulation of thyroid cells in Graves' disease. These findings support the results of the present study, which showed elevated TSHR gene expression in hyperthyroid patients [12].

Another study indicated that genetic and transcriptional variations in the TSHR gene may influence susceptibility to autoimmune thyroid diseases. Their findings suggested that increased expression or altered regulation of the TSHR gene could enhance immune recognition of thyroid cells, thereby contributing to disease development [10].

In contrast, the hypothyroid group in the present study showed relatively lower levels of TSHR gene expression compared with hyperthyroid patients. Hypothyroidism is often associated with autoimmune destruction of thyroid tissue, particularly in Hashimoto's thyroiditis, where immune-mediated damage leads to progressive loss of thyroid follicular cells. As thyroid tissue becomes damaged, the expression of functional thyroid receptors may decline, resulting in decreased responsiveness to TSH stimulation [9].

These findings are in agreement with the other study study which demonstrated that inflammatory processes and immune cell infiltration in Hashimoto's thyroiditis lead to structural and functional damage to thyroid tissue. Such damage may reduce the expression of thyroid-related genes, including TSHR [11].

Furthermore, immune-mediated cytokine signaling may influence the regulation of TSHR gene expression. Several cytokines produced during autoimmune responses, particularly those associated with the Th17 immune pathway, have been implicated in thyroid autoimmune diseases. Cytokines such as interleukin-23 (IL-23) contribute to the differentiation and maintenance of Th17 cells, which are known to promote inflammatory responses in autoimmune disorders [8]. These cytokines may indirectly regulate the transcription of genes involved in thyroid function, including TSHR.

Studies) have also reported that Th17-related cytokines are elevated in autoimmune thyroid diseases and may contribute to disease progression. The interaction between inflammatory cytokines and thyroid receptor signaling may therefore represent an important mechanism linking immune responses with thyroid dysfunction [5-7].

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